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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,083	11/19/2001	Zvi Cabantchik	A34366 PCT USA	5772
7590	06/28/2005		EXAMINER VENC, DAVID J	
Sol Sheinbein G.E. Ehrlich (1995) Ltd. c/o Anthony Castorina 2001 Jefferson Davis Highway Suite 207 Arlington, VA 22202			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/868,083	<b>Applicant(s)</b> CABANTCHIK ET AL.	
	<b>Examiner</b> David J. Venci	<b>Art Unit</b> 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on April 14, 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-5,8,9 and 11-21 is/are pending in the application.
- 4a) Of the above claim(s) 11-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5,8,9,20 and 21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-5,8,9 and 11-21 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

Examiner acknowledges Applicants' response filed April 14, 2005, which amended claims 1-5 and 8-9, cancelled claims 6-7 and 10, and added new claims 20-21.

Currently, claims 1-5, 8-9 and 20-21 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8-9 and 20-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants' have amended the following claims to recite limitations that are not supported by the disclosure, as originally filed:

Claim 1, step b) and step c), a "chelating-marker"

Claim 1, step b), a "chelating-marker chelating an additional metal ion"

Claim 1, step c) and d), a "chelating-marker not chelating said additional metal ion"

Claims 5 and 8, a "chelating marker"

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Claim 21, a method "wherein said non-bound metal ion and said additional ion are different"

Examiner is unable to find literal or contextual support for the aforementioned claim language in Applicants' specification and Applicants' argumentation presented in Applicants' response to the prior Office Action. Specifically, the recited "calcein" species found in the specification does not provide support for the broader genus "chelating marker." In addition, the recited passage allegedly found on page 1 of the application does not appear to provide support for the negative limitation of a "chelating-marker not chelating said additional metal ion."

Applicants are required to cancel the new matter in response to this Office Action.

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Claims 1-5, 8-9 and 20-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, step b), the recitation of "an additional metal ion" is indefinite because it is not clear whether "an additional metal ion" is derived from the sample. It is not clear whether step b) requires the step of chelating an additional metal ion from the sample.

In claim 1, step b) appears to contradict step c) and step d). Step b) recites "a chelating-marker chelating an additional metal ion" (emphasis added), while step c) and step d) recite a "chelating-marker not chelating said additional metal ion" (emphasis added). It is not clear whether the chelating-marker chelates an additional metal ion. It is not clear whether/what step(s) is/are missing between step b) and step c). It is not clear what step(s) is/are required in step d) for determining NTBI concentration "based on the amount of said chelating-marker not chelating said additional metal ion."

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In claim 3, the recitation of "desferrioxamine (DFO) polymer" is indefinite because it is not clear whether "desferrioxamine (DFO)" is a polymer-conjugated chelator by itself, or whether a separate polymer is conjugated to "desferrioxamine (DFO)."

***Claim Rejections - 35 USC § 103***

Claims 1-2, 5, 8-9 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skold et al. (US 5,334,513) in view of Breuer et al., 268 AM. J. PHYSIOL. C1354 (1995).

Skold et al. teach a method for determining the concentration of a non-bound metal ion (see col. 16, line 5, "metal ions") comprising the steps of: providing a surface (see col. 11, line 28, "support") coated with a polymer (see col. 11, lines 22-23, "synthetic or modified naturally occurring polymers") that is conjugated to a metal chelator (see col. 11, lines 31-32, "covalent bonding of reagents such as... chelating agents"), bringing a sample (see col. 23, line 39, "sample") into contact with said coated surface (see col. 23, lines 37-39, "forming a combination... of the sample... and the first reagent"), bringing into contact with said coated surface a marker (see col. 10, line 65, "Analog analyte", see col. 29, lines 20-23), determining the amount of marker not chelating said additional metal ions (see col. 28, lines 11-22), and determining the concentration of metal ion in the sample based on the amount of marker not chelating said additional metal ion (see col. 28, lines 11-22).

Skold et al. does not teach a "chelating-marker chelating an additional metal ion."

However, Breuer et al. teach the use of "chelating-marker chelating an additional metal ion" (see Abstract, "calcein") in iron assays (see Title). Therefore, it would have been obvious for a person of ordinary skill in the art to practice the method for determining the concentration of a metal ion, as taught by Skold et al.,

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with a "chelating-marker chelating an additional metal ion" because Breuer et al. discovered that Fe(II) caused 46% fluorescence quenching at a 4:1 iron:calcein ratio and "virtually complete" quenching at higher ratios (see p. C1356, col. 2). In addition, Breuer et al. discovered that Fe(III) caused "very rapid and potent" quenching when FeCl<sub>3</sub> is dissolved in distilled water. A person of ordinary skill in the art may interpret these results as an indication that calcein is a favorable indicator of iron concentration and, thus, would serve well in an assay for iron in a sample of serum or other biological fluids.

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Claims 3 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skold et al. (US 5,334,513) and Breuer et al., 268 AM. J. PHYSIOL. C1354 (1995), as applied to claims 1-2, and further in view of Yegorov et al., 15 FREE RADIC. BIOL. MED. 565 (1993).

Skold et al. and Breuer et al. describe a method for determining the concentration of a non-bound metal ion as substantially described supra. The aforementioned references do not teach a method incorporating "desferrioxamine (DFO) polymer" (claim 3) or a method wherein "said non-bound metal ion and said additional metal ion are different" (claim 21).

However, Yegorov et al. describe a method incorporating "desferrioxamine (DFO) polymer" (see Title, "desferal") and a method wherein "said non-bound metal ion and said additional metal ion are different" (see Title, "Fe(III) and Fe(II)"). Therefore, it would have been obvious for a person of ordinary skill in the art to use the method for determining the concentration of a non-bound metal ion, as taught by Skold et al. and Breuer et al., with "desferrioxamine (DFO) polymer" wherein "said non-bound metal ion and said additional metal ion are different" because Yegorov et al. discovered that accurate determination of non-bound metal iron requires a determination of both Fe(III) and Fe(II) simultaneously (see p. 568, col. 2, first sentence) and that desferrioxamine is capable of determining as little as 22  $\mu$ M of iron (see p. 572, paragraph bridging col. 1-2).

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Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Skold et al. (US 5,334,513) and Breuer et al., 268 AM. J. PHYSIOL. C1354 (1995), as applied to claim 1, and further in view of Guire & Chudzik (US 4,826,759).

Skold et al. and Breuer et al. describe a method for determining the concentration of a non-bound metal ion as substantially described supra. The aforementioned references do not teach a method incorporating a "multiwell plate."

However, Guire & Chudzik describe a "multiwell plate" (see Fig. 4) for metal ion determinations (see col. 4, line 23). Therefore, it would have been obvious for a person of ordinary skill in the art to use the method for determining the concentration of a non-bound metal ion, as taught by Skold et al. and Breuer et al., with a multiwell plate because Guire & Chudzik discovered a device that is "rapidly used to indicate the presence, and, if desired, to approximate the amount, of a particular analyte" and is "simple to operate, and can be used generally in the field by non-technical personnel having a minimum of training" (see col. 14, lines 1-16).

### ***Response to Arguments***

In prior Office Action, claim 5 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "marker is a fluorescent marker". Specifically, claim 5 was rejected because it was not clear how a fluorescent marker is "captured by the metal chelator" of claim 1. In response, Applicants have amended claim 5 to add the limitation of a "chelating marker." Notwithstanding issues of new matter under 35 U.S.C. 112, first paragraph, set forth supra, Applicants' amendment to claim 5 is sufficient to

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overcome claim rejection under 35 U.S.C. 112, second paragraph. Accordingly, claim rejection under 35 U.S.C. 112, second paragraph, is withdrawn.

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In prior Office Action, claims 1-5 and 9 were rejected under 35 U.S.C. 102(e) as being anticipated by Abuknesha (US 5,723,304). In addition, claim 8 was rejected under 35 U.S.C. 103(a) as being unpatentable over Abuknesha (US 5,723,304) in view of Breuer et al., 268 AM. J. PHYSIOL. C1354 (1995). In light of Applicants' claim amendments and argumentation, and in light of new claim rejections in view of Skold et al. (US 5,334,513), set forth supra, these rejections are withdrawn. Discussion pertaining to Abuknesha has been rendered moot.

With respect to Breuer et al., 268 AM. J. PHYSIOL. C1354 (1995), Applicants argue that calcein cannot be used as a primary iron detector alone, and that support-polymer conjugated DFO is also required (see Applicants' Remarks, p. 11, third full paragraph). Applicants' rebuttal is not persuasive because Applicants' rebuttal appears to merely restate Applicants' claimed invention and the inherent properties of calcein. Applicants have not adequately explained why it is not obvious to combine the teachings of Breuer et al. with the teachings of others.

### **Conclusion**

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final



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action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J Venci  
Examiner  
Art Unit 1641

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